SEQUENCE LISTING

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<110> Fainzilber, Michael M.
       Kits, Karel S.
       Burlingame, Alma L.
Olivera, Baldomero M.
Walker, Craig
       Watkins, Maren
       Shetty, Reshma
       Cruz, Lourdes J.
       Imperial, Julita
       Colledge, Clark
       University of Utah Resarch Foundation
       Vrije Universiteit
       Regents of the University of California
<120> Gamma-Conopeptides
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<150> US 60/069,706
<151> 1997-12-16
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<223> Xaa at residues 1, 2, 3, 4, 5, and 6 may be des-Xaa or any amino acid; Xaa at residues 8, 9,
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Xaa Xaa Xaa Cys Cys Xaa Xaa Xaa Xaa Cys Xaa Xaa Xaa Xaa Xaa
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Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa 35 <210> 3 <211> 39 <212> PRT <213> Artificial Sequence <220>... <223> Description of Artificial Sequence:generic formula of gamma-conopeptides <220> <221> PEPTIDE <222> (1)..(13) %<223> Xaa at residue 1 is any amino acid; Xaa at residues 2, 3, 4, 5 and 6 may be des-Xaa or any amino acid; Xaa at residues 8, 9, 10, 11, 12 and 13 may be any amino acid. · <220> <221> PEPTIDE <222> (27)..(39) <223> Xaa at residues 27, 28, 29, 31, 32, 33, 34, 35, 36 and 37 may be any amino acid; Xaa at residues 38 and 39 may be des-Xaa or any amino acid. <220> <221> PEPTIDE <222> (15)..(19) <223> Xaa at residues 15, 16, 17 and 18 may be any amino acid; Xaa at residue 19 is Glu or gamma-carboxyglutamate. <400> 3 Xaa Xaa Xaa Xaa Xaa Cys Xaa Xaa Xaa Xaa Xaa Cys Xaa Xaa Xaa Xaa Xaa Cys Cys Ser Asn Ser Cys Asp Xaa Xaa Xaa Cys Xaa Xaa 20 Xaa Xaa Xaa Xaa Xaa Xaa 35 <210> 4 <211> 39 <212× PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence:generic sequence of gamma-conopeptides. <220> <221> PEPTIDE <222> (1)..(13) <223> Xaa at residue 1 is any amino acid; Xaa at residues 2, 3, 4, 5 and 6 may be des-Xaa or any amino acid; Xaa at residues 8, 9, 10, 11, 12 and 13 may be any amino acid.

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      and 39 may be des-Xaa or any amino acid.
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Xaa Xaa

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 Ser Asn Ser Cys Asp Gln Thr Tyr Cys Xaa Leu Tyr Ala Phe Xaa Ser
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 Asp Xaa
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10 15 Asp Ser Xaa Cys Cys Ser Asn Ser Cys Asp Val Thr Arg Cys Xaa Leu 20 25 30 Met Xaa Phe Xaa Xaa Asp Xaa 35 <210>.9 <211> 27 <212>..PRT <213> Conus textile <220> <221> PEPTIDE <222> (1)..(27) <223> Xaa at residues 9, 13 and 17 are Glu or gamma-carboxyglutamate. <400> 9 Cys Lys Thr Tyr Ser Lys Tyr Cys Xaa Ala Asp Ser Xaa Cys Cys Thr Xaa Gln Cys Val Arg Ser Tyr Cys Thr Leu Phe <210> 10 <2.11> 34 <212> PRT <213> Conus textile <220> <221> PEPTIDE <222> (1)..(34) <223> Xaa at residues 2, 3, 10 and 32 are Trp or 6-bromo-Trp; Xaa at residues 18, 26 and 33 are Glu or gamma-carboxyglutamate; Xaa at residue 12 is Pro or hydroxy-Pro. <400> 10 Asp Xaa Xaa Asp Asp Gly Cys Ser Val Xaa Gly Xaa Cys Thr Tyr Asn . 1 Ala Xaa Cys Cys Ser Gly Asp Cys His Xaa Thr Cys Ile Phe Gly Xaa Xaa Val <210> 11 <211> 31 <212> PRT <213> Conus textile

<213> Conus textile

<220>
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 Xaa at residues 5, 18, 22 and 25 are Glu or
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 or hydroxy-Pro.

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Glu Arg Ala Lys Ile Asn Leu Leu Pro Lys Arg Lys Pro Pro Ala Glu
cgt tgg ttg gaa tgc agt gtt tgg ttt tca cat tgt acg aag gac tcg
                                                                    96
Arg Trp Leu Glu Cys Ser Val Trp Phe Ser His Cys Thr Lys Asp Ser
gaa tgt tgt tct aat agt tgt gac caa acg tac tgc acg tta atg cca
                                                                    144
Glu Cys Cys Ser Asn Ser Cys Asp Gln Thr Tyr Cys Thr Leu Met Pro
ccg gac tgg tgacatcgcc actctcctgt tcagagtctt caaggctttt
                                                                    193
Pro Asp Trp
 · /, 50
gttctctttt gaagaatttt aacgagtgaa caaaaaagtg gactagcatg tttccttttc 253
cctttgcaaa atcaatgatg gaggtaaaag cctcccattt tgtcttcatc aataaagaac 313
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 Glu Cys Cys Ser Asn Ser Cys Asp Gln Thr Tyr Cys Thr Leu Met Pro
 Pro Asp Trp
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                                        Met Glu Lys Leu Thr Ile Leu
 ctt ctt gtt gct gct gta ctg ttg tcg atc cag gcc cta aat caa gaa
                                                                     163
 Leu Leu Val Ala Ala Val Leu Leu Ser Ile Gln Ala Leu Asn Gln Glu
 aaa cac caa cgg gca aag atc aac ttg ctt tca aag aga aag cca cct
                                                                     211
 Lys His Gln Arg Ala Lys Ile Asn Leu Leu Ser Lys Arg Lys Pro Pro
 get gag egt tgg tgg egg tgg gga gga tge atg get tgg ttt ggg ett
                                                                     259
 Ala Glu Arg Trp Trp Arg Trp Gly Gly Cys Met Ala Trp Phe Gly Leu
 40
 tgt tcg agg gac tcg gaa tgt tgt tct aat agt tgt gac gta acg cgc
                                                                     307
Cys Ser Arg Asp Ser Glu Cys Cys Ser Asn Ser Cys Asp Val Thr Arg
 tgć gag tta atg cca ttc cca cca gac tgg tgacatcgac actctcctct
                                                                     357
 Cys Glu Leu Met Pro Phe Pro Pro Asp Trp
               7.5
                                   80
 tcagagtctt caaggctttt gttctctttt gaagaatttt tacgagtgaa caaaaacgtg 417
 gactagcacg tttccttttc cctttgcaaa atcaatgatg gaggtaaaag tgtcccattt 477
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	Ile Gln A	la Leu 20	Asn	Gln	Glu	Lys	His 25	Gln	Arg	Ala	Lys	Ile 30	Asn	Leu	
	Leu Ser L	ys Arg 35	Lys	Pro	Pro	Ala 40	Glu	Arg	Trp	Trp	Arg 45	Trp	Gly	Gly	
	Cys Met A 50	la Trp	Phe	Gly	Leu 55	Cys	Ser	Arg	Asp	Ser 60	Glu	Cys	Cys	Ser	
	Asn Ser C	ys Asp	Val	Thr 70	Arg	Cys	Glu	Leu	Met 75	Pro	Phe	Pro	Pro	Asp 80	
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	gta ctg at Val Leu Mo	tg tcg et Ser 15	acc Thr	cag Gln	gcc Ala	atg Met 20	ttt Phe	caa Gln	ggt Gly	gat Asp	gga Gly 25	gaa Glu	aaa Lys	tcc Ser	99
	cgg aag go Arg Lys A														147
	aag cag aa Lys Gln Ly 45														195
	gaa tgc to Glu Cys C														243
	tgaattcgg	a ccaca	agcc	a to	cgat	atca	ccc	ctct	cct	cttc	agaç	gc t	tcaa	ggctt	303
•	ttgttatcc	t tttga	aagaa	t ct	ttat	cgaç	, taa	acat	aag	taga	caag	ıct t	:tttt	tttcc	363
	tttgcaaaa	t gaaga	aatga	t gg	caaa	aago	ccc	ccat	ttt	gtct	tcat	ca a	taaa	gaact	423
	cgctatcag														441
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Leu Thr Ile Leu Leu Val Ala Ala Val Leu Met Ser Thr Gln Ala
                         10
cta att caa gat caa cgc caa aag gca aag atc aac ttg ttt tca aag
                                                                   153
Leu Ile Gln Asp Gln Arg Gln Lys Ala Lys Ile Asn Leu Phe Ser Lys
aga cag gca tat gct cgt gat tgg tgg gac gat ggc tgc agt gtg tgg
                                                                   201
Arg Gln Ala Tyr Ala Arg Asp Trp Trp Asp Asp Gly Cys Ser Val Trp
                 40
ggg cct tgt acg gtg aac gca gaa tgt tgt tct ggt gat tgt cat gaa
                                                                   249
Gly Pro Cys Thr Val Asn Ala Glu Cys Cys Ser Gly Asp Cys His Glu
acg tgc att ttc ggg tgg gaa gtc tgaccacaaa ccatccgaca tcgccactct
Thr Cys Ile Phe Gly Trp Glu Val
cctcttcaga gacttcaagg cttttgttct cttttgaaga attttacgag tgagcaaaaa 363
ggtagactag cacgtttctt tttccctttg caaaatcaat gatggaggta aaagcctccc 423
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Ser Val Trp Gly Pro Cys Thr Val Asn Ala Glu Cys Cys Ser Gly Asp
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                                                      Met Glu Lys
ctg aca atc ctg ctt ctt gtt gct gct gta ctg atg tcg acc cag gcc
                                                                   166
Leu Thr Ile Leu Leu Val Ala Ala Val Leu Met Ser Thr Gln Ala
ctg gtt gaa cgt gct gga gaa aac cac tca aag gag aac atc aat ttt
                                                                   214
Leu Val Glu Arg Ala Gly Glu Asn His Ser Lys Glu Asn Ile Asn Phe
tta tta aaa aga aag aga gct gct gac agg ggg atg tgg ggc gaa tgc
                                                                   262
Leu Leu Lys Arg Lys Arg Ala Ala Asp Arg Gly Met Trp Gly Glu Cys
aaa gat ggg tta acg aca tgt ttg gcg ccc tca gag tgt tgt tct gag
Lys Asp Gly Leu Thr Thr Cys Leu Ala Pro Ser Glu Cys Cys Ser Glu
gat tgt gaa ggg agc tgc acg atg tgg tgatgaattc tgaccacaag
                                                                   357
Asp Cys Glu Gly Ser Cys Thr Met Trp
ccatctgaca tcaccactct cctcttcaga ggcttcaagg cttttgtttt cctttttgaat 417
aatctttacg agtaaacaaa taagtagact agcgcgtttt tttccctttg agaaatcaat 477
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 Ile Asn Phe Leu Leu Lys Arg Lys Arg Ala Ala Asp Arg Gly Met Trp
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Cys Ser Glu Asp Cys Glu Gly Ser Cys Thr Met Trp
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                                       10
ctg att caa ggt ggt ggt gac aaa cgt caa aag gca aac atc aac ttt
                                                                   97
Leu Ile Gln Gly Gly Gly Asp Lys Arg Gln Lys Ala Asn Ile Asn Phe
ctt tca agg tgg gac cgt gag tgc agg gct tgg tat gcg ccg tgt agc
                                                                   145
Leu Ser Arg Trp Asp Arg Glu Cys Arg Ala Trp Tyr Ala Pro Cys Ser
cct ggc gcg caa tgt tgt agt ttg ctg atg tgt tca aaa gcg acc agc
Pro Gly Ala Gln Cys Cys Ser Leu Leu Met Cys Ser Lys Ala Thr Ser
cgc tgc ata ttg gcg tta tgaactctga ccacaagcca tccqacatca
                                                                   241
Arg Cys Ile Leu Ala Leu
ccactctcct cttcagaggc ttcaaggctt tttgtttttc ttttgaagaa tctttacgag 301
tgaacaaata agtagaatag cacgtttttc cccctttgca aaatcaataa tggaggttaa 361
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Leu Ser Lys Gly Lys Thr Asn Ala Glu Arg Arg Asn Gly Gln Cys Glu 35 40 45

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Cys Glu Met Tyr Cys Thr Gln Ile Gly

65. 70

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ccg acc cag gcc ctt ttt caa ggt gat gac gga aaa tcc cag aag gcg
Pro Thr Gln Ala Leu Phe Gln Gly Asp Asp Gly Lys Ser Gln Lys Ala
                 20
                                                                   144
gag atc aag tct ttt gaa aca aga aag tta gcg aga aac aag cag gta
Glu Ile Lys Ser Phe Glu Thr Arg Lys Leu Ala Arg Asn Lys Gln Val
cgc tgc ggt ggt tgg tca acg tat tgt gaa gtt gac gag gaa tgc tgt
                                                                   192
Arg Cys Gly Gly Trp Ser Thr Tyr Cys Glu Val Asp Glu Glu Cys Cys
                                                                   241
tcg gaa tca tgt gta agg tct tac tgc acg ctg ttt gga tgaactcgga
Ser Glu Ser Cys Val Arg Ser Tyr Cys Thr Leu Phe Gly
                         70
ccacaagcca tccgatatca ccactctcct gttcagagtc ttcaag
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<213> Conus marmoreus
<400> 31
Met Glu Lys Leu Thr Ile Leu Leu Leu Val Ala Ala Val Leu Ile Pro
Thr Gln Ala Leu Phe Gln Gly Asp Asp Gly Lys Ser Gln Lys Ala Glu
Ile Lys Ser Phe Glu Thr Arg Lys Leu Ala Arg Asn Lys Gln Val Arg
Cys Gly Gly Trp Ser Thr Tyr Cys Glu Val Asp Glu Glu Cys Cys Ser
     50 .
Glu Ser Cys Val Arg Ser Tyr Cys Thr Leu Phe Gly
                     70
<210> 32
<211> 278
<212> DNA
<213> Conus marmoreus
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<221> CDS
<222> (4)..(213)
<400> 3.2
atc atg cag aaa ctg ata att ctg ctt ctt gtt gct gct gtg ctg atg
   Met Gln Lys Leu Ile Ile Leu Leu Leu Val Ala Ala Val Leu Met
acg acc cag gcc cta tat caa gaa aaa cgc cga aag gag atg atc aat
Thr Thr Gln Ala Leu Tyr Gln Glu Lys Arg Arg Lys Glu Met Ile Asn
                                                                   144
ttt tta tca aaa gga aag ata aat gct gag agg cgg aac ggc gga tgc
Phe Leu Ser Lys Gly Lys Ile Asn Ala Glu Arg Arg Asn Gly Gly Cys
                                                                   192
aaa gct act tgg atg tct tgt tca tcg ggc tgg gaa tgc tgt tct atg
Lys Ala Thr Trp Met Ser Cys Ser Ser Gly Trp Glu Cys Cys Ser Met
agt tgt gac atg tac tgc gga tagataggat gaactctgac cacaagccat
                                                                   243
Ser Cys Asp Met Tyr Cys Gly
                                                                   278
ccgacatcac cactctcctc ttcagagtct tcaag
<210> 33
<211> 70
<212> PRT
<213> Conus marmoreus
<400> 33
Met Gln Lys Leu Ile Ile Leu Leu Leu Val Ala Ala Val Leu Met Thr
Thr Gln Ala Leu Tyr Gln Glu Lys Arg Arg Lys Glu Met Ile Asn Phe
Leu Ser Lys Gly Lys Ile Asn Ala Glu Arg Arg Asn Gly Gly Cys Lys
Ala Thr Trp Met Ser Cys Ser Ser Gly Trp Glu Cys Cys Ser Met Ser
Cys Asp Met Tyr Cys Gly
<210> 34
<211> 528
<212> DNA
<213> Conus textile
<220>
<221> CDS
<222> (98)..(316)
<400> 34
gcacgtcatc ttctctctca gtctgcctga cagctgcctt cagtcaaccc tgccgtcatc 60
tcagcgtaga cttggtaaga agtgaaaaac atttatc atg cag aaa ctg ata atc
                                         Met Gln Lys Leu Ile Ile
```

```
ctg ctt ctt gtt gct gct gtg ctg atg tcg acc cag gcc gtg ctt caa
                                                                 163
Leu Leu Val Ala Ala Val Leu Met Ser Thr Gln Ala Val Leu Gln
             10
                                 15
gaa aaa cgc cca aag gag aag atc aag ctt tta tca aag aga aag aca
                                                                 211
Glu Lys Arg Pro Lys Glu Lys Ile Lys Leu Leu Ser Lys Arg Lys Thr
gat gct gag aag cag cag aag cgc ctt tgc ccg gat tac acg gag cct
                                                                 259
Asp Ala Glu Lys Gln Gln Lys Arg Leu Cys Pro Asp Tyr Thr Glu Pro
tgt tca cat gcc cat gaa tgc tgt tca tgg aat tgt tat aat ggg cac
                                                                 307
Cys Ser His Ala His Glu Cys Cys Ser Trp Asn Cys Tyr Asn Gly His
tgt acg gga tgaactcgga ccacaagcca tccgacatca ccactctcct
                                                                 356
Cys Thr Gly
cttcagaggc ttcaagactt ttgttctgat tttggacaat ctttacgagt aaacaaataa 416
ttagactage acttttttc ccctttgcaa aatcaatgat ggaggtaaaa agcctcccat 476
<210> 35
<211> 73
<212> PRT
<213> Conus textile
<400> 35
Met Gln Lys Leu Ile Ile Leu Leu Leu Val Ala Ala Val Leu Met Ser
Thr Gln Ala Val Leu Gln Glu Lys Arg Pro Lys Glu Lys Ile Lys Leu
Leu Ser Lys Arg Lys Thr Asp Ala Glu Lys Gln Gln Lys Arg Leu Cys
Pro Asp Tyr Thr Glu Pro Cys Ser His Ala His Glu Cys Cys Ser Trp
Asn Cys Tyr Asn Gly His Cys Thr Gly
<210> 36
<211> 26
<212> PRT
<213> Conus textile
<220>
<221> PEPTIDE
<222> (1)..(26)
<223> Xaa at residue 18 is Trp or 6-bromo-Trp; Xaa at
     residues 7 and 14 are Glu or
     gamma-carboxyglutamate; Xaa at residues 3 and 8
     are Pro or hydroxy-Pro.
<400> 36
Leu Cys Xaa Asp Tyr Thr Xaa Xaa Cys Ser His Ala His Xaa Cys Cys
 1
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Ser Xaa Asn Cys Tyr Asn Gly His Cys Thr

<210> 41

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20
<210> 37
<211> 4
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:consensus
      gamma-conopeptide sequence for probe
<220>
<221> PEPTIDE
<222> (1)
<223> Xaa is Glu or Gln.
<400> 37
Xaa Cys Cys Ser
  1.
<210> 38
<211> 12
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:degenerate
     probe for consensus gamma-conopeptide sequence.
<400>, 38
sartgytgya gy
                                                                    12
<210> 39
<211> 12
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence:degenerate
      probe for consensus gamma-conopeptide sequence.
<400> 39
sartgytgyt cn
                                                                    12
<210> 40
<211> 8
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence:consensus
      pro-gamma-conopeptide sequence for probe.
<400> 40
Ile Leu Leu Val Ala Ala Val Leu
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24

```
<211> 24
 <212> DNA
 <213> Artificial Sequence
 <220>
 <223> Description of Artificial Sequence: degenerate
     probe for consensus pro-gamma-conopeptide
    sequence.
 <400> 41
athytnytng tngcngcngt nytn
 <210> 42
 <211> 32
 <212> PRT
 <213> Conus pennaceus
 <220>
 <221> PEPTIDE
 <2223 (1)..(31)
 <223> Xaa at residues 14 and 26 are
    gamma-carboxyglutamate; Xaa at residue 31 is hdroxy-Pro.
 <400> 42
Asp Cys Thr Ser Trp Phe Gly Arg Cys Thr Val Asn Ser Xaa Cys Cys
Ser Asn Ser Cys Asp Gln Thr Tyr Cys Xaa Leu Tyr Ala Phe Xaa Ser
              20
<210> 43
<211> 27
<212> PRT
<213> Conus textile
<220>
<221> PEPTIDE
<222> (1)..(27)
<223> Xaa at residues 9 and 13 are
      gamma-carboxyglutamate.
<400> 43
Cys Gly Gly Tyr Ser Thr Tyr Cys Xaa Val Asp Ser Xaa Cys Cys Ser
Asp Asn Cys Val Arg Ser Tyr Cys Thr Leu Phe
             20
                                  25
<210> 44
<211> 8
<212> PRT
<213> Conus pennaceus
<220>
<221> MOD_RES
<222> (2)
<223> Xaa at residue 2 is carboxymethylCys
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```
<400> 44
Asp Xaa Thr Ser Trp Phe Gly Arg
<210> 45
<211> 24
<212> PRT
<213> Conus pennaceus
<220>
<221> PEPTIDE
<222> (1)..(24)
<223> Xaa at residues 6 and 18 are
      gamma-carboxyglutamate; Xaa at residue 23 is
      hydroxy-Pro.
<400> 45
Xaa Thr Val Asn Ser Xaa Xaa Xaa Ser Asn Ser Xaa Asp Gln Thr Tyr
                   5
                                        10
Xaa Xaa Leu Tyr Ala Phe Xaa Ser
<210> 46
<211> 18
<212> DNA
<21:3> Artificial Sequence
<220>
<223> Description of Artificial Sequence:primer for M13
      universal priming site.
<400> 46
tttcccagtc acgacgtt
                                                                       18
<210> 47
<211> 19
<212> DNA
<213> Artificial Sequence
<223> Description of Artificial Sequence:primer for M13
      reverse priming site.
<400> 47
cacacaggaa acagctatg
                                                                      19
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